machines cost up to US$400,000. And although the IonWorks platform works well for voltage-gated channels, where you can adjust the voltage at the same time as recording, it will not work for fast ligand-gated channels, whose currents often last a millisecond or less, as the machine cannot add test compounds and record simultaneously.

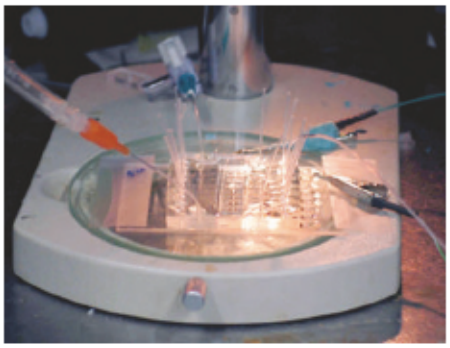
Contenders aiming to overcome the ligand-gated channel barrier in automated patch clamping also include Sophion Bioscience of Ballerup, Denmark, which uses a microfluidics approach. Its QPatch 16 operates 16 independent patch-clamp sites, each comprising a flat silicon chip with recording electrodes, a patch-clamp hole, pipetting wells and integrated microfluidic glass flow channels for applying solutions. "QPatch 16 also provides a cell preparation facility in which the cells are suspended in culture medium until right before the experiment. This ensures that cells are kept viable and healthy, and enables unattended operation for at least 4 hours," says Niels Willumsen, a senior executive at Sophion. The integrated microfluidic flow channels of the QPlate allow sequential application of multiple compounds at very low volumes (around 5 μl) from four to eight pipette tips, and ensure the fast solution exchange (about 50 ms) required to study ligand-gated ion channels. The modular design can be upgraded to a 48-channel system and the machine can give 250–1,200 data points per working day.

On a smaller scale, Fred Sigworth and Kathryn Klemic at Yale University, New Haven, Connecticut, have developed a planar patch clamp that can be built in the lab. "In the future, instead of buying an expensive chip, a lab might have a little device that can make an electrode, or an array of little electrodes, by moulding them out of silicon rubber," says Sigworth. A thin layer of polydimethylsiloxane (PDMS) resin is poured on to a plate containing a 2-μm diameter hole. Before the PDMS cures, air is blown through the hole, creating a 1-μm hole in the rubber sheet. After peeling the sheet off the plate, exposure of the surface to plasma oxidation creates a 100-μm thick glassy surface layer of SiO_2. "On the one hand you have a hydrophobic silicone rubber base, then you create this thin layer of glass that the cell rests on — to a cell it looks a lot like a conventional glass electrode," says Klemic.

In expert hands, the best systems for patch clamping can currently detect a pulse of about 150 elementary charges: equivalent to a flow of 150 sodium ions. "The grand challenge would be to resolve single elementary charges. Then you could watch a lot of really interesting processes such as the turnover of ions in pumps," says Sigworth. He is unsure whether this single-ion resolution will ever be possible, but thinks that it may be possible to mould the PDMS sufficiently carefully to reduce the capacitance in the system and substantially increase the resolution.

NANION

Nanion's Port-a-Patch makes patch clamping easy for the novice.



F. SIGWORTH & K. KLEMIC

Do-it-yourself: the PDMS microfluidic patch-clamp system in use.

Sigworth is also intrigued by the Port-a-Patch system developed by Nanion Technologies, a spin-off from the Centre for Nanoscience at the University of Munich in Germany. The beauty of Port-a-Patch is its ease of use. "It's basically a bench-top patch clamp. You pipette in the cells, close the lid and make the recording," he says. Nanion claims that this turn-key solution only takes half an hour to set up. "We run one-day training courses, and the system is easily used by people who have no experience in electrophysiology," says Nanion's

BANKING ON STEM CELLS

Human stem cells are valuable commodities: as well as their medical potential, their pristine naivety makes them attractive as gold-standard cell lines for research. Stem-cell banks, where owners deposit their precious products and would-be investigators apply for loans, are now being developed.

The most advanced is the UK Stem Cell Bank, based at the National Institute for Biological Standards and Controls in Potters Bar, near London. Initiated in September 2002, and funded by the Medical Research Council and the Biotechnology and Biological Sciences Research Council since January 2003, it has the aim of providing a repository for all types of human stem-cell lines.

"As of October 2005, we have 24 stem-cell lines approved for accession into the bank," says director Glyn Stacey, but none is yet ready for sending out to end-users. That probably won't be until early 2006. "The process is complex. It is not like growing an ordinary cell line where you could create and quality control a bank within a few months of receiving the cells," says Stacey. One time-consuming step is the creation of agreements for depositers and recipients, with each cell type presenting different problems and opportunities. Exploitation will be controlled by the depositer who retains ownership of the cells.

Legal issues aside, stem cells are challenging to grow. The main problem is scaling up to provide hundreds of ampoules of cells at identical passage levels and stages of differentiation. "It could take an entire day for a highly skilled person to dissect and recover cells from just one line," says Stacey. And cultures have to be characterized and checked for contamination before release.

All lines currently in the bank are human embryonic stem (ES) cells. "We have had some contact with people who think they have adult stem cell lines, but they are being careful about characterization," says Stacey.

MRC

Glyn Stacey: stem cells are challenging to grow.

A few ampoules of each cell line have been frozen as back-up, whereas the master bank contains 20 or 30 ampoules. The distribution stock may eventually contain around a hundred ampoules of each line. Stacey hopes that early in 2006 the bank's website will start tracking progress of the cell lines that will be available to researchers.

A few other initiatives are taking shape. The US National Stem Cell Bank will be located at the WiCell Research Institute, in Madison, Wisconsin, with a $16.1 million, four-year National Institutes of Health grant. It will acquire, store, characterize and distribute human embryonic stem-cell lines, but will be limited to those approved for federal funding. After a year of legal wrangling, a stem-cell bank is taking shape at the University of Granada in Spain, and others are being considered in Australia and South Korea. P.M.